Original Research Article

Study of Mast Cells in Non Neoplastic Skin Conditions

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Abstract

Introduction: Mast cells are always been a fascinating field of research workers working with inflammatory processes, Hypersensitive disorders, and hosts defence mechanisms. Wide variation in mast cell counts and blood density is noticed in different sections of the skin in same biopsy sample.
Aim and objectives: To assess the pattern of mast cell arrangement in various non- neoplastic skin lesions and compared with normal skin biopsies, to analyze the pattern of mast cell distribution in various non-neoplastic lesions of the skin, to compare with quantum of mast cells in various non-neoplastic lesions.
Materials and methods: A study was conducted for 10 years from March 2006 to February 2016, which included all non-neoplastic skin conditions were subjected for mast cell count and distribution in the Department of Pathology at Gandhi Medical College/ Hospital with collaboration with Dermatology Department. The biopsy specimens were processed and stained with routine H&E and special stain for mast cells Toluidine Blue. The mast cells counted with the help of ocular micrometer under the microscope.
Results: About 1000 non-neoplastic lesions grouped into 11 categories and mast cell count was done. Irrespective of the category, Urticaria pigmentosa showed highest mast cell count (144/sqmm). Nevus comedonicus showed lowest count (13/sqmm).
Conclusion: The role of mast cells in health and disease is significant and distinct alterations of mast cell are present in various non-neoplastic conditions.

Key words

Mast cells, Ocular micrometer, Urticaria Pigmentosa, Nevus comidonicus.

Introduction

Mast cells are always been a fascinating field of research workers working with inflammatory process, hypersensitive disorders and host's defence mechanism [1]. Mast cells are derived from bone marrow and are found primarily in the dermis of skin, gastro intestinal mucosa, upper and lower respiratory tract and conjunctiva [1, 2]. Mast cell precursor is a pluripotent (CD34+) stem cell that resides in the bone marrow, after leaving the bone marrow it circulates enters the tissues and undergoes local differentiation and maturation with expression of particular proteases and proteoglycans [3]. They are spindle shaped cells with oval nucleus and contain numerous granules in their cytoplasm which do not stain with routine Hematoxylin and Eosin stain, but stain with special stains which include, Toluidine Blue, methylene blue and Alcian Blue and shows Metachromasia, i.e.; the granules stain in a color which is different from that possessed by the dye and appear red rather than blue.

Mast cells are found in all levels of the dermis, but predominantly located at the vicinity of the dermoepidermal junction [6], and also in the subcutaneous tissue. Increased number is observed perivascularly, perineurally and periadnexally and the estimated density of 7000 to 20000 mast cells per cubic mm of skin [1]. They are mixed with lymphocytes and histiocytes in close apposition to fibroblasts. It is very difficult to distinguishing them with the routine H&E stain [4, 5]. The number of mast cells increases at inflammatory sites in atopic dermatitis, psoriasis, rheumatoid synovitis and inflammatory bowel disease.

There are increased numbers of mast cells observed in the younger age group (20-25 years), and higher in females. Wide variation in mast cell counts and blood vessel density is noticed in different sections from the same biopsy sample. This confirms the notion that mast cells are unevenly distributed [7] this variation is taken into consideration in the study of mast cells i inflammatory skin disease [11]. Skin mast cells are different from intestinal and lung mast cells. All mast cells respond to severe stimuli and produce prostaglandin's PGD2, but leukotriene 4 is not produced by dermal mast cells.

The role of mast cells in disease is significant and distinct alterations of mast cells are present in various non-neoplastic skin lesions. During the acute inflammatory conditions the tissue mast cells decrease in number and may disappear temporarily. Later as the acute process subsides increase in the number of mast cells is noticed.

Materials and methods

The present study was the prospective study undertaken in the Department of Pathology in collaboration with Department of Dermatology at Gandhi Medical college/Hospital Secunderabad from 2004 – 2018. Around 1000 patients registered and diagnosed as non- neoplastic inflammatory of developmental or metabolic were subjected to various lab tests including histological biopsy examination. The biopsy specimens were put in formalin fixative and processed by routine paraffin embedding technique, as mast cell demonstration does not require paraffin embedding technique. 5 micrometer tissue sections were cut from the paraffin tissue blocks and were stained with 2 staining techniques i.e. Routine H and E section and Toludine blue stain.

Mast cell counting Technique

All the Toluidine Blue stained sections were screened under low, high power and oil immersion objectives.

The mast cells were counted in 10 high power fields (HPF) 40X were counted by summing up the total mast cells in 10 fields and calculating average number of mast cells obtained. Ocular

micrometer diameter was 0.47mm hence the radius of one field was 0.235 mm.

The area of 1 hpf was (Per square) i.e. 22/7 (0.235) square i.e. approximately 0.2 sqmm to derive the number of mast cells per high power field the cells counted in high power field (i.e. per 0.2 sqmm) is multiplied by 5. The mast cells were expressed in terms of cells per sqmm area of the tissue sections. Thus the mast cells in various non – neoplastic skin lesions of the present study were quantified and compared with each group.

Results

Toluidine blue method

The mast cells appear as oval cells present in all the levels of dermis. They contain blue nucleus and dense purple granules. Among the various biopsies in different patients of age groups i.e. 0-20, 21 – 40, 41 – 60 and above age group, females outnumbered males in the proportion of 53:47. 100 non neoplastic skin lesions were grouped into 11 categories and the mean mast cells are counted. Irrespective of the category Urticaria pigmentosa showed highest mean mast cell count (144/sq.mm), nevus commedonicus showed the lowest (13/sq.mm). The largest number of mast cells was seen in the bacterial infections (38/sq.mm) and the lowest in vascular diseases (21/sq.mm).

Age and sex distribution of study cases was as per **Table – 1**. Mean mast cells counts in non-neoplastic skin lesions were as per **Table – 2**. Photomicrographs were as per **Figure – 1 to 7.**

Table - 1: Age and sex distribution of study cases.

Age group (Years)	Males	Females	Total
0-20	130	120	25
21-40	210	312	52
41-60 and above	127	101	23
Total	467	533	1000

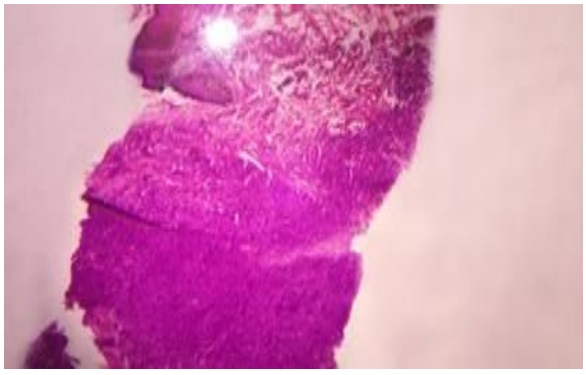
Table - 2: Mean mast cells counts in non-neoplastic skin lesions.

Category of Disease	No. of cases	Mean Mast Cells/ mm^2
Bacterial infections	21	38
A] Leprosy	16	92.25
1] Tuberculoid leprosy	03	35
2] BorderlineTuberculoid	08	33
3] Indeterminate	02	14
4] Lepromatous leprosy	03	41
B] Tuberculosis	05	42.5
1] Lupus vulgaris	03	30
2] Tuberculosis verrucosa cutis	02	55
Vesicular Bullous lesions	10	29.2
A] Pemphigus vulgaris	04	27
B] Pemphigus foliaceous	02	3
C] Bullous Pemphigoid	02	34.5
D]Transientacantholytic dermatitis	01	31
E] Erythroderma	01	19
Papular Squamous lesions	19	31.7
A] Lichen planus	11	27
B] Psoriasis	03	29
C] Para psoriasis	01	44
D] Pityriasis Rubra pilaris	01	29
E] Prurigo nodularis	02	35
F] Lichen nitidus	01	26
Connective tissue disorders	18	24
A] Morphea	08	17.5
B] Scleroderma	04	33
C] Erythema nodosum	03	44
D] Panniculitis	01	29
E]Lichen sclerosis at Atrophicus	02	35
Metabolic diseases of skin	02	28.5
A] Lichen Amyloidosis	01	36
B] Porphyria cutanea tarda	01	21
Vascular diseases	03	21
A] Pyoderma gangrenosum	01	13
B] Angio keratoma	02	29
Non inflammotry-granuloma Granuloma annulare	02	28.5

Cutaneous toxicities of drugs Acute generalized erythematous pustules	01	35
Inflammatory Diseases of epidermal appendages	09	32
A] Alopecia areata	04	27
B] Pseudo palade of Broq	01	41
C] Folliculitis	04	27
Congenital diseases	03	36
A]Nevus Sebaceous of Jadosshan	01	19
B] Nevus depigmentoses	01	28
C] Ectodermal dysplasis	01	31
Others	12	331.5
A] Urtcaria pigmentosa	01	144
B] Epidermal nevus	02	82.5
C] Vitiligo	01	29
D] Pityriasis alba	01	31
E] Seborrhic keratosis	01	34
F] Acne keloidalis nuchae	01	44
G]Polymorphous light eruption	03	27
I] Achrochordan	01	55

Bacterial infections: leprosy and tuberculosis: highest mast cell count was observed in lepromatous leprosy (41/sq.mm). Lowest mast cell count was observed in indeterminate hansen's (19/sq.mm) in tuberculosis, lupus vulgaris shows arrangement of mast cells periadenexally and perivascularly with 50% of liberation of granules.

Figure – 1: Photomicrograph of lepromatous leprosy showing (H & E, 10X); and showing perivascular mast cells in the inflammatory cell infiltrate (Toluidine Blue, 100X).



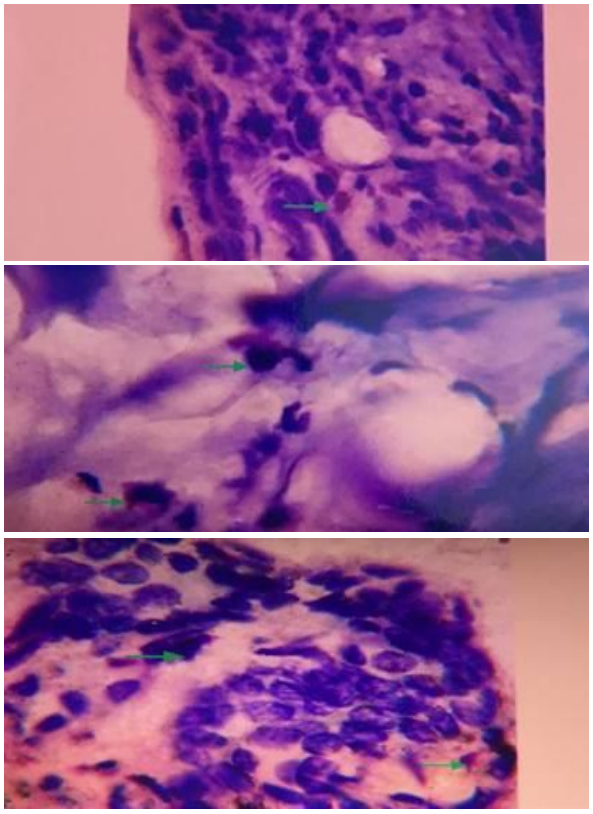
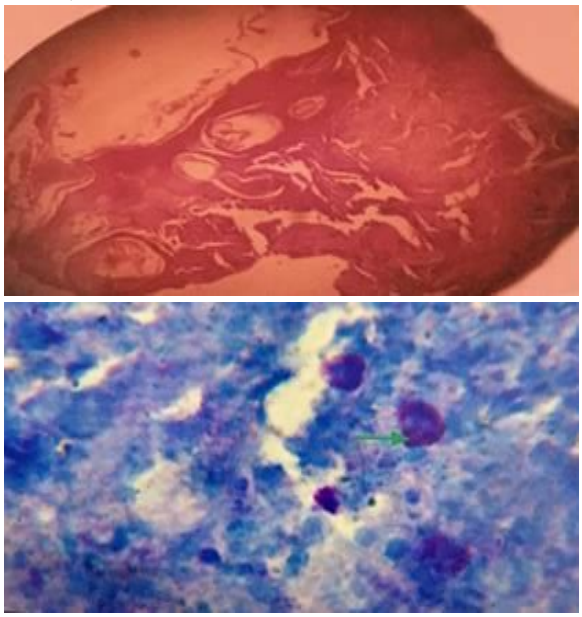


Photo – 2: Photomicrograph of tuberculosis verrucosa cutis with dermal tuberculoid granulomas (H & E, 4X) and (Toluidine Blue, 100X).



Papulo squamous lesions: psoriasis – perivascular and periadenexal mast cells are seen. In lichen planus – 50% of liberation of granules and perivascular arrangement of mast cells are seen.

Figure - 3: Photomicrograph of Psoriasis showing mast cells in the inflammatory cell infiltrate (H & E, 10X) and (Toluidine Blue, 100X).

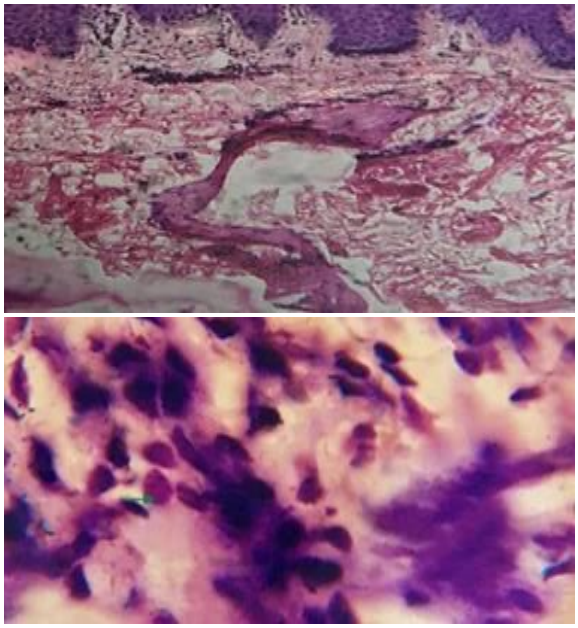
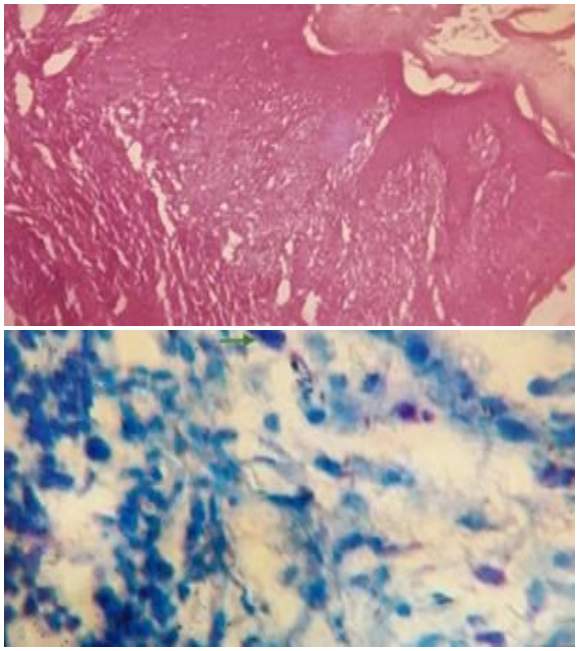


Figure - 4: Photomicrograph of Lichen planus with mast cells in the inflammatory cell infiltrate (H & E) (Toluidine Blue, 100X).



Vesicular bullous lesions: mast cells are seen in the papillary dermis with perivascular and periadenexal arrangement.

Connective tissue disorders: in Morphea mast cells are found in the reticular dermis with peri vascular arrangement. In erythema nodosum mast cells are found in papillary dermis with 40% liberation of granules.

Figure – 5: Photomicrograph of Lichen nitidus showing mast cells with liberation of granules in the inflammatory cell infiltrate (H & E) and (Toluidine Blue, 100X).

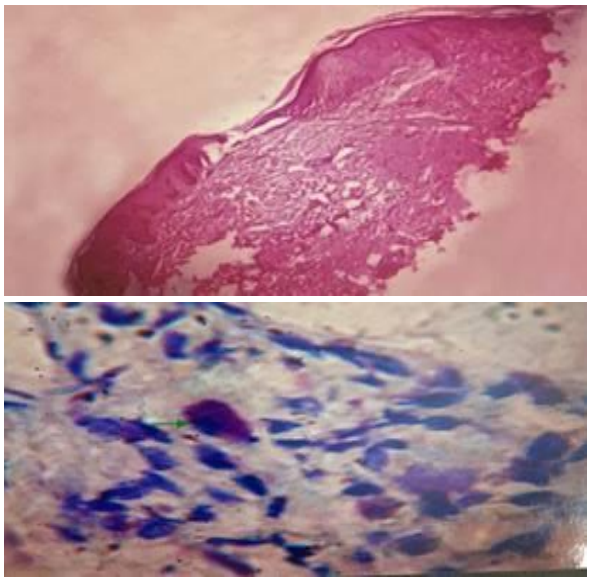
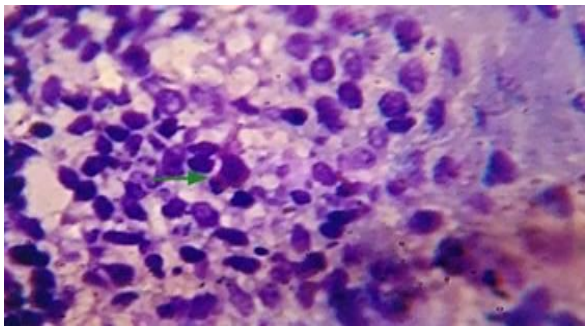


Figure – 6: Photomicrograph of liichen sclerosis et atrophies with mast cells in inflammatory ccell infiltrate in the dermis (Toluidine Blue, 100X).



Metabolic diseases of skin: mast cells are mostly arranged perivascularly in both papillary and reticular dermis.

Vascular diseases: mast cells are arranged perivascularly with 40% liberation of granules.

Granuloma annuare: mast cells are arranged peri adenexally.

Cutaneous toxicities of drugs: mast cells are arranged perivascularly.

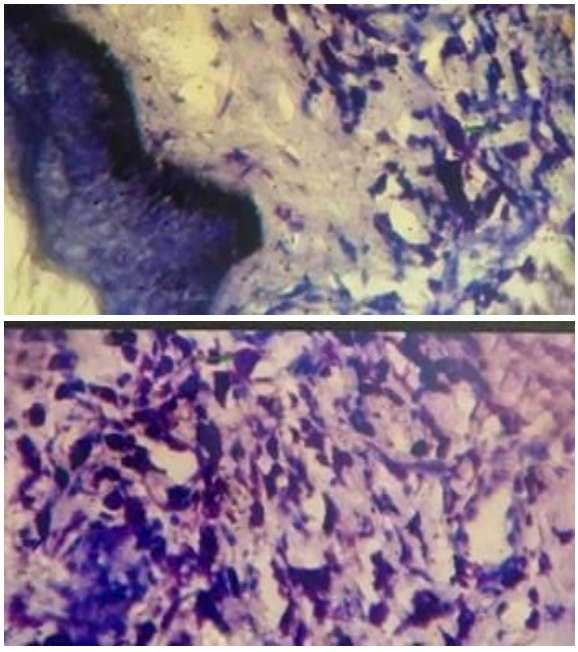
Inflammatory diseases of epidermal appendages: in alopecia areata mast cells are arranged perivascularly and periadenexally, in

folliculitis mast cells are arranged perivascularyly.

Congenital diseases: in nevus sebaceous of jadosshan; mast cells are arranged perivasculary with 50% liberation of granules. In ectodermal dysplasia 30% of mast cells are liberating granules.

Others: In epidermal nevus mast cells are arranged perivascularly and periadenexally with more than 50% liberating granules. In vitiligo mast cells are perivascular with more than 30% are liberating granules. In Urticaria pigmentosa, the mast cells are arranged periadenexally with 50% liberating granules.

Figure – 7: Photomicrograph of Urticaria pigmentosa with extensive inflammatory cell infiltrate in the dermis comprising of mat cells and dermal inflammatory cell infiltrate



Discussion

Mast cells have been a fascinating riddle of researchers and are involved in inflammatory processes, hypersensitive disorders and host defence mechanisms. Skin being one of the easily biopsied tissues and involved by numerous non neoplastic conditions and contains mast cells, serve as an example to study mast cells. Mast cells of the skin are found at all levels of dermis where they are grouped around blood vessels, nerves, appendages and sub cutaneous tissues.

Mast cells are always sparsely located and focally distributed. The counting of the cells has been subjected to variation [1, 11]. The present study has adopted an unbiased methodology by counting mast cells in 5 fields, each on either side of a tissue section with the help of ocular micrometer and expressed in terms of mast cells/sq.mm area of the tissue sections quantified as the mast cells can be easily identified by high over view as done in other studies [1, 11].

In the present study there is significant variation of mast cell numbers in different types of lesions. Mast cells predominated in infective conditions, than in congenital lesions as similar to the observation of others [1, 11]. Highest number of mast cells was seen in Urticaria pigmentosa (144/sq.mm), and lowest in Nevus commidonicus (13/sq.mm). In infective conditions, Leprosy shows highest number of mast cells (mean mast cell count is 38/sq.mm) and more number are seen in lepromatous leprosy in comparison with tuberculoid leprosy.

Rav, et al. [12], and Aroni, et al. [13], observed a trend for mast cells to be decreasing from lepromatous to the tuberculoid end of the spectrum. They felt that the mast cells did not appear to stay long in the lesion at the tuberculoid end of the spectrum, unlike in lepromatus lesion. They cited two reasons for this, firstly the life span of mast cells is varied from weeks to months and secondly it is possible that the reduction of mast cell density occurs when the lesion changes to tuberculoid type with changes in the cytokine patterns.

Jayalakshim, et al. [14] counted statistically more significant difference between mast cell count in treated and untreated lepromatous patients. Chowdhary and Ghosh [15] count frequent changes in size and shapes of mast cells, swelling, degranulation with less dense stain in tuberculoid leprosy with reaction compared to lepromatous leprosy without reaction. There is

no role for mast cells in the pathogenesis of leprosy but the mast cell count might help in predicting stability of the lesion.

In Lupus vulgaris, mast cells are arranged perivascularly and periadenexally whereas tuberculosis verrucosa cutis has shown only perivascular distribution similar to the study by Rav, et al. [12].

In vesiculo bullous lesions mast cells are high in bullous pemphigoid (35/sq.mm) and are arranged in perivascularly and periadenexally.

Mast cell distribution varies among lichenoid lesions with lichen planus shows perivascular arrangement, and lichen plano pilaris shows periadenxal location. But Naukkerinen, et al. [16] count mast cells in close apposition with dermal nerve in lichen planus. Walton and Desouza [11] count more mast cells in fascia and arm skin among lichen planus lesions, and they thought the variation in age, sex an site to be an influencing factor for the mast cell count.

Mast cells are increased in the early stages of scleroderma and morphea, but tend to decrease as the lesion progress [17]. In the present study there were 3 cases of scleroderma which were in early stage and showed mast cells around dermal vessels and in the subcutaneous tissue. Mean mast cell count is 33/sqmm and there are 7 cases of morphea in late sclerotic stages showed less number of mast cells (17.5/sq.mm).

The role of mast cells in health and disease is significant and distinct alteration of mast cells is present in various non-neoplastic skin lesions. During acute inflammatory conditions the tissue mast cells decrease in number and many disappear temporarily, later as the acute process subside and proceed to chronic stage then occurs progressive increase in number of mast cells in affected area [1]. Therefore increase in mast cell count has been observed in various non-neoplastic skin lesions like lichen planus, scleroderma and pephigus vulgaris and others.

Since the mast cell is enzymatically active cell, it is necessary to study the role of mast cell in the pathogenesis of various inflammatory/ non inflammatory non neoplastic lesions of the skin.

Conclusion

- In the present study included total of 1000 skin biopsies from the Dermatology department over a period of 10 years and processed at the Dept. of Pathology in Gandhi Hospital.
- The biopsied specimen were processed and stained with H & E stain and 2% aqueous Toluidine blue stain. With the Toluidine blue method, the mast cells appeared as oval cells with blue nucleus and dense purple granules in all the levels of dermis.
- They were counted and mean mast cell count was expressed in terms of sq.mm area of tissue sections with the help of occulomicrometer. Various non-neoplastic skin lesion of present study were quantified and compared with each group. Higher no. of lesions was found in 20 to 40 years age group and females outnumbered males.
- The lesions were grouped into 11 categories. In bacterial infections leprosy showed highest mast cell count in the sub type of lepromatous leprosy. In connective tissue disorders increased no. of mast cells were seen in early stages of scleroderma and morphea, but decreased in the late stages.
- The role of mast cells in health and disease was significant and distinct alteration of mast cells are present in various non-neoplastic skin lesions.
- Since the mast cell is enzymatically active cell, it is necessary to study the role of mast cell in the pathogenesis of various inflammatory/ non inflammatory non neoplastic lesions of the skin.

References

1. Ramdas Naik, Mukta Ramesh, Alurnima, Baligna Bantwal, Shankara Narayan A. Study of mast cells in non-neoplastic skin lesions. Indian Jr. of Pathology, Microbiology, 2003; 46(2): 173-75.
2. Irwin. M. Freedberg, Arthur. Z Eisen, Thoas B. Fitz Patric (Eds), Text book of Fitz Patrick's dermatology in General Medicine, 5th edition, 1999, Vol.1, Chapter 34, p. 414-20.
3. David Elder, Rosalie Elenitsas, Christine Jaworsky (Eds), Lever's Histopathology of skin, 8th edition, Philadelphia, 1997, p. 31-33.
4. Marshall J.S., Ford G.P., Bell E.B. Formalin sensitivity and differential staining of mast cells in human dermis. British Journal of Dermatology, 1987; 117: 29-36.
5. Lavker RM, Kligman A.M. Chronic Heliodermatitis: A morphologic evaluation of chronic dermal damage with emphasis on the role of mast cells. J. Invest. Dermatol., 1988; 325-29.
6. Cowen T, Trigg P, Eady F.A.J. Distribution of mast cells in human dermis. Br. J. Dermatol, 1979; 100: 635-40.
7. R.A.J. Eady, Lowen T, Marshall T.F., Plummer V, Greaves M.W. Mast cell population density, blood vessel density and histamine content in normal human skin. British Journal of dermatology, 1979, 100: 623-32.
8. Lawrence I.D, Warner J.A., Victoria L.C., Hubbard W.C., Kagey-Sabotka A., Lichnestein L.M. Purification and characterization of human skin mast cells, evidence for human skin mast cell heterogeneity. Jr. Immunol., 1987; 139: 3062-69.
9. Michelson G, Kraaz W. The skin and the gut in psoriasis. actaderm venerol., 1997 Sept.; 77(5): 343-46.
10. Toruniowa B., Jablanska S. Mast cells in initial stages of psoriasis. Arch. Dermatol. Res., 1988; 280; 189-93.
11. Walton S, Desouza E.J. Variation in mast cell numbers in psoriasis and lichen planus-comparison with normal skin. Dermtologica, 1983; 166: 236-39.
12. Rav S.D., Pratap V.K., Sarma N.K., Dayal S.S. Mast cells in leprosy. Indian J. Lepr., 1990; 62: 467-72.
13. Aroni K., Konto Chicopoulos G., Liossi A., Panteloes D. An investigation of mast cells in two basic leprosy groups. Int. Jr. epr. Other Mycobacterial diseases, 1993; 61: 634-35.
14. Jayalakshmi P, Lian T.K., Mast cells in lepromatous leprosy (Letter to the editor) Int. Jr. Lepr. Other Mycobacterial diseases; 1995; 63: 291-93.
15. Chaudhary S.K., Ghosh S. Distributon of mast cells in "reaction in tuberculoid leprosy". Bull Calcutta Trop Med, 1968; 13-14.
16. Naukkerinen A., Harvima I.T., Aalto M.L, et al. Quantitative analysis of contact sites between mast cells and sensory nerves in cutaneous psoriasis and lichen planus based on a histochemical double staining technique. Arch. Deratol Res., 1991; 283: 433-37.
17. Greenberg G., Burnstock G. A novel cell to cell interaction between mast cells and other cell types. Experimental cell research, 1983; 147: 1-13.